Remarks

In the present application claims 1-14, 16-19, 22 and 47-56 are pending. Claims 47-56 have been found to be allowable by the Examiner and claims 1-14, 16-19 and 22 are again presented for the Examiner's review and consideration. Claim 15 is canceled herein.

Claims 1 and 22 were rejected under 35 USC 102 as being anticipated by Tomich et al. Similarly, claims 1, 4, 6, 8, 9, 13, 19 and 22 were rejected under 35 USC 102 as being anticipated, in the alternative, by Ma *et al.* or Chan *et al.* These rejections are respectfully traversed. Independent claims 1, 2 and 22 are amended herein to include the recitation previously presented in claim 15 (now canceled) that the pores of the claimed substrate are "between 0.5μm and 10 μm" in diameter. Neither Tomich, Ma nor Chan disclose such specific pore sizes. Tomich does not disclose any particular pore size and Ma and Chan disclose dramatically larger pore sizes of 500-700 μm and 300 μm, respectively.

Regarding Tomich, the shield referred to therein is not a porous substrate as indicated by the Examiner. The shield is disclosed as a protective layer that "can be placed across the fragile lipid bilayer to protect the bilayer from disturbance from external influences." (Col. 19, lns. 61-63). Rather than a porous substrate for creating a high resistance seal, only a traditional patch pipette is actually disclosed. (Fig. 15). This is clearly described as "a biosensor based generally on the single channel pipette device widely used in ion channel studies." (Col. 14, lns. 45-65). Based on this description, the aperture or space referred to in Tomich, at col. 19, line 45, would at most be understood by a person skilled in the art to be either a prior art perforated film such as disclosed in Ma and Chen (and with similarly sized pores) or, more likely, the tip of a conventional patch pipette as shown in Fig. 15. For these reasons, none of the cited references anticipate independent claims 1, 2, or 22 as amended herein, nor any of the claims dependent thereon.

The rejection of claims 1-19 and 22 under 35 U.S.C. 103(a) as unpatentable over Chan *et al.* in view of Olesen *et al.* is also respectfully traversed. As recognized by the Examiner, Olesen discloses the use of a conventional patch pipette 62. Even assuming the Examiner to be correct, that the membrane of Chan could be substituted for the conventional

pipette of Olesen, the combination still does not meet the claims as amended due to the dramatically larger pore size of Chan as explained above.

However, applicants to do not agree that the proposed combination of Chan and Olesen is even appropriate and further traverse on these grounds. First, the cells addressed in Olesen are physically much smaller than the cells used with the apparatus of Chan. Therefore, to be useful with the Olesen apparatus, the Teflon membranes disclosed in Chan would need to be significantly changed in pore size. There is, however, no teaching for such a change. Moreover, the Examiner proposes that the modification be made such that the Chan substrate be made of glass rather than Teflon as disclosed. However, it is well known by persons skilled in the art that glass substrates have been previously investigated as substrates for apparatus of the type disclosed by Chan and have been rejected as unsuitable in such devices. Thus, not only is there a lack of motivation for the proposed combination, there is a counter motivation against such a modification. Because there is no motivation for the proposed combination and because the combination, even if made, would not meet the claim limitations, independent claims 1, 2 and 22, as well as the claims dependent thereon are patentable over the cited references.

In view of the foregoing amendments and remarks, the application as a whole is believed to be in form for allowance and its earliest possible allowance is earnestly solicited. The Examiner is invited to call the undersigned attorney at (415) 442-1106, if a telephone call could help resolve any remaining items.

Respectfully submitted,

Date: November 15, 2004

51,743

Shawn C. Glidden (Reg. No.)

For:

Thomas D. Kohler (Reg. No. 32,797)
Morgan, Lewis & Bockius LLP
Two Palo Alto Square
3000 El Camino Real
Palo Alto, California 94306
(415) 442-1106